PDCN: 88940000127

DOW CORNING

May 23, 1995

TSCA Document Processing Center (TS-790)
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Attn: TSCA Section 8(e) Coordinator
401 M Street S.W.
Washington, D.C. 20460

Re: Supplemental Submission to 8EHQ-94-1
TSCA Section 8(e) Notification of Substantial Risk
Triethoxysilane

8EHQ-0595-12885

Dear Sir:

In accordance with the provisions of Section 8(e) of the Toxic Substances Control Act (TSCA), as interpreted in the Statement of Interpretation and Enforcement Policy (40 FR 11110, March 16, 1978), Dow Corning Corporation is submitting the following final report as a supplemental submission to our Notification of Substantial Risk of September 9, 1994 (8EHQ-94-12885).

Chemical Substance:

CASRN 998-30-1 Triethoxysilane

Contains No CBI

Manufacturer:

Dow Corning Corporation
2200 West Salzburg Road
Midland, Michigan 48686-0994

ORIGINAL

Submitted Study:

ACUTE INHALATION TOXICITY EVALUATION ON TRIETHOXYSILANE IN RATS

Dow Corning Corporation
January 11, 1995

Background:

In a letter dated September 9, 1994, Dow Corning Corporation provided EPA with a Notification of Substantial Risk under TSCA §8(e) concerning preliminary results obtained in an ongoing acute inhalation toxicity study on triethoxysilane in rats. As promised in our letter, at this time we are providing the Agency with a copy of the final toxicological report as a supplemental submission to our original notification of substantial risk (8EHQ-94-12885).

Executive Summary:

The test substance, chemically identified as triethoxysilane (CASRN 998-30-1) was administered as a vapor to two groups of five male and five female Fischer CDF® (F-44)/CrlBR albino rats for four hours at mean vapor concentrations of 0.5 and 1.3 mg/l, respectively.

Clinical signs of toxicity observed in the 0.5 mg/l dose group included excessive lacrimation and decreased activity noted immediately post-exposure while gasping, wheezing, labored breathing, decreased activity, and, with one female, death on day 13, were observed during the 14-day post-exposure observation period.

Clinical signs of toxicity observed in the 1.3 mg/l dose group included excessive lacrimation and decreased activity noted immediately post-exposure, while gasping, wheezing, labored breathing, corneal opacity, excessive lacrimation, decreased activity, and, with all animals, death, were observed during the 14-day post-exposure observation period.

Pharmacotoxic signs for both dose groups increased in number and severity during the post-exposure observation period. All animals in the lower dose group lost weight during the first post-exposure observation week. During the second post-exposure week, males began regaining weight but did not attain their group mean pre-exposure weight, while females continued to lose weight. All surviving animals in the higher dose group lost weight during the first post-exposure week, none of these animals surviving to the 14-day post-exposure body weight measurement.

At necropsy, red discolored lungs were observed in four of ten animals from the 0.5 mg/l dose group and in all animals from the 1.3 mg/l dose group.

Based on the results of this study, the four-hour median concentration (LC_{50}) in rats exposed to triethoxysilane vapor is between 0.5 mg/l and 1.3 mg/l.

Actions:

Dow Corning will notify EPA of any further pertinent information that may be developed concerning this chemical substance.

If you require further information concerning this notification of substantial risk, please contact Dr. Rhys G. Daniels, Regulatory Compliance Specialist, Dow Corning Product Safety and Regulatory Compliance Department, at the address provided below or by telephone at 517-496-4222.

If you require further information concerning the toxicology of triethoxysilane, please contact Dr. Richard W. Mast, Director of Toxicology and Bioscience Research, at the address provided below or by telephone at 517-496-8569.

Sincerely,

Alvin E. Bey

Alvin E. Bey
U.S. Area Vice-President
Corporate Director HES

RGD050699.WP

DOW CORNING

Contains No CBI

TSCA SECTION 8(e) NOTIFICATION OF SUBSTANTIAL RISK

TOXICOLOGICAL STUDIES

TSCA CONFIDENTIAL BUSINESS INFORMATION CLAIMS

For purposes of Notification of Substantial Risk under Section 8(e) of the Toxic Substances Control Act (TSCA), the general PROPRIETARY designation on the attached toxicological study has been waived by Dow Corning Corporation.

Submitter: _____ Date: 23 May 1995

Rhys G. Daniels, Ph.D.
Regulatory Compliance Specialist
Health and Environmental Sciences
DOW CORNING CORPORATION

DOW CORNING

ACUTE INHALATION TOXICITY EVALUATION OF TRIETHOXYSILANE IN RATS

Dow Corning Corporation
January 11, 1995

Contains No CBI

Acute Inhalation Toxicity Evaluation on Triethoxysilane in Rats

TEST ARTICLE: Triethoxysilane

PERFORMING LABORATORY: IRDC
500 North Main Street
Mattawan, MI 49071
616/668-3336

LABORATORY PROJECT IDENTIFICATION: 416-098

AUTHOR: Roger J. Hilaski, M.A.

SPONSOR: Dow Corning Corporation
2200 West Salzburg Road
Auburn, MI 48611

DATE OF STUDY COMPLETION: December 27, 1994

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1. QUALITY ASSURANCE STATEMENT

This study was reviewed in accordance with the United States Environmental Protection Agency Toxic Substances Control Act Good Laboratory Practice Standards 40 CFR Part 792 effective September 18, 1989 and the Organization for Economic Cooperation and Development Principles of Good Laboratory Practice adopted May 12, 1981.

Below are the inspections conducted by the IRDC Quality Assurance Department and the dates the inspections were reported to the Study Director and Management:

Date(s) of Inspection	Study Phase Inspected	Date(s) Reported to Study Director/ Management
6/29/94	Protocol Review	6/30/94
7/28/94	Body Weight Measurement	10/17/94
10/19/94-10/25/94	Report Review	10/25/94
10/19/94-10/25/94	Data Review	10/25/94
11/04/94-11/07/94	Report Review	11/08/94
12/22/94-12/23/94	Report Review	12/27/94

Theresa A. Stewart, B.Sc.
Manager, Quality Assurance

12/27/94
Date

2. SUMMARY

This study was conducted according to the OECD Guidelines for Testing of Chemicals, Section 4, No. 403, "Acute Inhalation Toxicity" adopted May 12, 1981 and the United States EPA (TSCA) Good Laboratory Practice Standards 40 CFR Part 792 effective September 18, 1989.

Two groups of 5-male and 5-female albino rats were exposed for four hours using whole-body exposure methods to mean vapor concentrations of 0.5 and 1.3 mg/L, for Groups 1 and 2 respectively, of triethoxysilane. An aerosol particle size determination was conducted for each group but a negligible amount of material was collected. Therefore, it was judged that no aerosols were present during the exposure.

One female exposed to 0.5 mg/L and all the animals exposed to 1.3 mg/L died prior to study termination. However, no animals were dead immediately post-exposure. Pharmacotoxic signs for both groups increased in number and severity during the post-exposure observation period. The significant signs noted immediately post-exposure for the animals exposed to 0.5 mg/L were excessive lacrimation and decreased activity. During the 14 day post-exposure period, the animals exposed to 0.5 mg/L exhibited the following significant pharmacotoxic signs: gasping, wheezing, labored breathing, decreased activity and one death.

Immediately post-exposure, animals exposed to 1.3 mg/L exhibited excessive lacrimation and decreased activity as the significant pharmacotoxic signs. Significant signs observed during the 14 day post-exposure observation period for animals exposed to 1.3 mg/L were gasping, wheezing, labored breathing, corneal opacity, excessive lacrimation, decreased activity and death.

All the animals exposed to 0.5 mg/L lost weight during the first post exposure observation week. During the second post-exposure week males started regaining weight but did not attain their group mean pre-exposure weight and females continued to lose weight.

All surviving animals exposed to 1.3 mg/L lost weight during the first post-exposure week; none of these animals survived to the 14 day post-exposure body weight measurement.

At necropsy, red, discolored lungs was the significant observation in four of ten animals exposed to 0.5 mg/L and ten of ten animals exposed to 1.3 mg/L. Based on the results of this study the four hour LC_{50} in rats exposed to triethoxysilane is between 0.5 mg/L and 1.3 mg/L.

3. INTRODUCTION

3.1. OBJECTIVE

The purpose of this study was to evaluate the acute toxicity of an experimental compound when administered via the inhalation route according to the Guidelines of the Organization for Economic Cooperation and Development (Acute Inhalation Toxicity, No. 403) issued May 12, 1981 and the Environmental Protection Agency: Toxic Substances Control Act Test Guidelines, Part 798 - Health Effects Testing Guidelines, subpart B., Section 798.1150, September 1985.

3.2. STUDY SCHEDULE

Study Initiated	Group Number	Date of Exposure	Date of Final Observation
6-20-94	1	7/21/94	8/04/94
	2	8/09/94	8/22/94

4. MATERIALS AND METHODS

4.1. TEST ARTICLE

The test article was received from the Dow Corning Corporation on July 1, 1994. The pertinent test article information is located in Appendix A.

4.2. EXPERIMENTAL DESIGN

Two groups of five male and five female albino rats were exposed to vapor atmospheres of triethoxysilane for four hours as measured from the end of the T_{99} equilibration time using whole body exposure methods. After exposure, surviving animals were held for a 14-day observation period. All animals underwent a complete necropsy. The following summary shows the experimental design of this study:

Group Number	Desired Concentration (mg/L)	Number of Animals	
		Male	Female
1	slightly greater than 0.5	5	5
2	1.3	5	5

4.3. TEST SYSTEM

4.3.1. Species

Rat

4.3.2. Strain

CDF® (F-344)/CrlBR
Fischer

4.3.3. Source

Charles River Kingston
RTE 209
Stone Ridge, NY. 12484

4.3.4. Reason for Selection

The rat was selected as the test system because it is a universally used model for demonstrating acute toxicity.

4.3.5. Body Weight Range

Male weights ranged from 179 - 207 grams and females ranged from 129 - 135 grams on the day of exposure.

4.3.6. Age at Start of Study

66 days for Group 1 animals, 57 days for Group 2 animals.

4.3.7. Method of Identification

Ear tag

4.3.8. Quarantine

Group 1 animals were acclimated for a period of 16 days. Group 2 animals were acclimated for a period of seven days.

4.3.9. Housing

Individual stainless steel wire mesh cages.

4.3.10. Environmental Conditions (Quarantine and Post-Exposure Periods)

Animal room with controlled temperature, humidity and light (12 hours light and 12 hours dark) was maintained in accordance with the recommendations contained in the D.H.H.S. Publication entitled "Guide for the Care and Use of Laboratory Animals"

4.3.11. Selection for Study

Selected from a colony maintained for acute work based on body weight and the appearance of good health.

4.3.12. Diet

Certified Pelleted Rodent Chow® #5002, Purina Mills, Inc., St. Louis, Missouri. was provided *ad libitum* except during exposure.

4.3.13. Water

Tap water was supplied *ad libitum* except during exposure.

4.4. TEST ARTICLE ADMINISTRATION

4.4.1. Animal Exposure

The animals were exposed to vapor atmospheres of the test article for four hours (measured from the end of the T_{99} chamber equilibration time) in a 160 liter stainless steel and glass exposure chamber. Chamber ventilation air was provided by the compressed air system used to generate the vapor and dilution air.

4.4.2. Generation of Exposure Atmospheres

Vapor atmospheres of the test article were generated using a system similar to that shown in Figure 1. The test article was metered via a syringe drive (Harvard Model 22) to a glass vaporization column (2.5cm diameter x 22cm height) filled approximately three-quarters full with glass beads ranging from 4-6mm in diameter. The test article is delivered to the center of the glass beads where compressed air entering the base of the column at 20 L/min, measured by a flow meter (Fischer & Porter, FP-1-27-G-10/55), facilitates vaporization. The test material is swept through a condensation trap and into the exposure chamber. Additional dilution air measured by a flowmeter (Fischer & Porter, FP-3/4-21-G-10/55) was used to decrease the vapor concentration to the desired level. The test atmosphere was exhausted to a fume hood. The generation system operational parameters are summarized below:

	Harvard Syringe Drive				
Group Number	Syringe Type	Syringe Diameter (mm)	Liquid Flow Rate (ml/min)	Air Flow Rate (L/min) (Column)	(Dilution)
1	Hamilton	14.57	0.02	20	20
2	Hamilton	32.6	0.069	20	30

4.5. DETERMINATION OF EXPOSURE CONCENTRATIONS

4.5.1. Nominal Exposure Concentrations

The nominal exposure concentration for each group was calculated by dividing the total amount of test article used during the generation by the total volume of air passed through the chamber.

4.5.2. Actual Exposure Concentrations

Exposure atmospheres were measured using infrared spectrophotometer (IR) analysis methods (Wilks Miran 1A Model 5688). The IR response was recorded with a chart recorder (Linear, model 156). The test material, triethoxysilane, was used to develop a calibration curve relating known concentrations of triethoxysilane to recorder chartlines. The calibration curve was developed using closed loop injections into the IR. Table 1 summarizes the IR calibrations for Groups 1 and 2.

On the day of exposure the IR system stability was verified by conducting a single-point calibration check.

Exposure atmospheres were monitored by drawing a continuous sample from the exposure chamber.

Actual concentrations were determined from the strip chart recording. Concentrations, taken from the strip chart at 15 minute intervals were tabulated and the mean ppm concentration calculated for the exposure. The ppm concentration was converted to mg/L.

Table 2 presents the instrument parameters for the IR and the chart recorder.

4.5.3. Particle Size Determinations

To assure the absence of aerosolized test material in the chamber a sample of the exposure atmosphere was collected to determine the particle size distribution. The sample was collected with an Andersen® 8-stage cascade impactor. The chamber was sampled at 28.3 L/min. The amount of aerosol collected on each stage was determined gravimetrically. The cumulative percentages, by weight, of particles with aerodynamic diameters smaller than the cutoffs for the individual stages of the impactor were derived and plotted by computer. The mass median aerodynamic diameter (MMAD) and geometric standard deviation (GSD) were calculated by a method similar to that of Raabe (Environ. Sci. Technol., 12: 1162-1167, 1978).

4.6. APPEARANCE, BEHAVIOR AND MORTALITY

Observed for pharmacotoxic signs pre-exposure and immediately after exposure; two times daily during the 14-day post-exposure period, once for pharmacotoxic signs and once for mortality only. The use of the computerized data collection system (Xybion) required body weights and observations to be identified such that day 1 is the day of exposure and days 2-15 are post-exposure days 1-14.

4.7. BODY WEIGHTS

Body weights were recorded just prior to the exposure, and at 7 and 14 days post-exposure and when animals were found dead.

4.8. NECROPSY

All animals were euthanized by intraperitoneal sodium pentobarbital overdose and exsanguination via the abdominal aorta and underwent a complete necropsy. All major organs in abdominal and thoracic cavities were observed for gross abnormalities by veterinary pathologists. No tissues were retained.

4.9. DATA RETENTION

All raw data, documentation, records, protocols, and final reports generated as a result of this study will be retained at IRDC (500 N. Main Street, Mattawan, MI 49071) and will be made available for inspection upon request by authorized personnel of the Sponsor for a period of 5 years following study completion (final report issue date).

5. RESULTS

5.1. EXPOSURE ATMOSPHERE CHARACTERIZATION

5.1.1. Nominal Exposure Concentration

Nominal exposure concentration results are presented in Table 3.

5.1.2. Actual Exposure Concentration

Nominal versus mean actual concentrations agreed very closely which is typical for vapor atmosphere exposures. The comparisons are 0.5 versus 0.5 mg/L for Group 1 and 1.2 versus 1.3 mg/L for Group 2. Actual exposure concentration results are presented in Table 4.

5.1.3. Particle Size Distribution

The exposure atmosphere was judged to have no aerosols present. Negligible amounts were collected during the sampling for the particle size determination.

5.2. ENVIRONMENT

Temperature, relative humidity and chamber airflow were monitored continuously during the exposure and recorded at 30 minute intervals. In addition, the oxygen content of the exposure atmosphere was measured once during the exposure. Mean environmental conditions in the chamber remained constant throughout the exposure at 24°C, 2% relative humidity, 40 L/min airflow and 20.8% oxygen for Group 1 and 23°C, 6% relative humidity, 50 L/min airflow and 21% oxygen for Group 2. The details of these measurements are shown in Table 5. The low relative humidity resulted from the dry compressed air used to generate the vapor. The post exposure room temperature ranged between 19 and 22°C and the relative humidity ranged between 44 and 70%.

5.3. BEHAVIOR AND MORTALITY (See Appendix B):

For animals exposed to 0.5 mg/L the significant pharmacotoxic signs noted immediately post-exposure were excessive lacrimation and decreased activity. During the two week post-exposure period the significant pharmacotoxic signs observed for these animals were death, gasping, labored breathing, slow respiration, decreased activity and wheezing.

Significant pharmacotoxic signs noted immediately post-exposure for animals exposed to 1.3 mg/L were decreased activity and excessive lacrimation. During the post exposure period the significant signs observed for animals exposed to 1.3 mg/L were death, decreased activity, labored breathing, wheezing, corneal opacity, gasping and excessive lacrimation.

No animals were dead immediately post-exposure from either group, however one female exposed to 0.5 mg/L was found dead on study day 13. All of the animals exposed to 1.3 mg/L died by post exposure day 13. A list of mortalities by study day are in Table 6.

5.4. BODY WEIGHTS (See Appendix C)

All animals exposed to 0.5 mg/L lost weight during the first post-exposure observation week (approximately 13% for males and 11% for females) based on mean group body weight. During the second post-exposure week, the males started regaining the lost weight but did not attain their group mean pre-exposure weight and the females continued to lose weight (approximately 18% for the total 14 days) based on mean group body weight. All surviving animals exposed to 1.3 mg/L lost weight during the first post-exposure week (approximately 19% for males and 11% for females) based on mean group body weight. None of the Group 2 animals survived for 14 day post exposure body weight evaluation. The body weight data are summarized in Table 8. Body weights for animals found dead are listed in Table 7.

5.5. NECROPSY (See Appendix D)

One male and three females exposed to 0.5 mg/L were observed with red discoloration of the lung ranging from trace to moderate. All animals exposed to 1.3 mg/L exhibited red discoloration of the lung ranging from mild to severe. No other significant macroscopic abnormalities were observed.

6. SIGNATURES

Prepared By: _____ 12/23/94
Jeffrey J. Bruce, B.S.
Group Supervisor,
Inhalation Toxicology
Date

Reviewed By: _____ 12-23-94
Bennie A. Culp
Department Manager,
Inhalation Toxicology
Date

Reviewed By: C.E. Ulrich Dec. 22 94
Charles E. Ulrich, B.S.
Director,
Inhalation Toxicology
Date

7. STUDY DIRECTOR'S STATEMENT

There were no significant deviations from the Good Laboratory Practice Standards which affected the quality or integrity of the study. This study was conducted in conformance with the EPA TSCA Good Laboratory Practice Standards 40 CFR Part 792 effective September 18, 1989 and the OECD Principles of Good Laboratory Practice adopted May 12, 1981. Comments on Study Data are presented in Appendix F. This report accurately reflects the raw data obtained during the performance of the study.

Roger Hilaski 12-27-94

Roger J. Hilaski, M.A.
Staff Toxicologist,
Inhalation Toxicology
Study Director

Date

Table 1. Infrared Spectrophotometer Closed-Loop Calibration

Group 1

Injection Volume Triethoxysilane (μL)	Closed-Loop Volume (L)	Calculated Concentration (ppm)	Resulting Calibration Chartlines
2	5.7	50	32
3	5.7	76	42
4	5.7	101	49
6	5.7	152	63

Group 2

Injection Volume Triethoxysilane (μL)	Closed-Loop Volume (L)	Calculated Concentration (ppm)	Resulting Calibration Chartlines
4	5.7	101	31.0
8	5.7	203	51.5
12	5.7	304	64.5

Table 2. Instrument Parameters

	Group 1
Infrared Spectrophotometer	
Type	Wilks Miran 1A-CVF
Model	5688
Analytical Wavelength	9.0 microns
Path Length Setting	1.82
Response Time Setting	1 Second
Gain Switch Setting	X10
Gain Setting	5.78
Range Setting	1 absorbance
Slit Width	1 mm
Cell Pressure	-1 psig
Strip chart Recorder	
Type	Linear
Model	156
Range	1 Volt = 100 chartlines
Chart Speed	30 cm/hour

	Group 2
Infrared Spectrophotometer	
Type	Wilks Miran 1A-CVF
Model	5688
Analytical Wavelength	9.2 microns
Path Length Setting	1.35
Response Time Setting	1 Second
Gain Switch Setting	X10
Gain Setting	3.66
Range Setting	1 absorbance
Slit Width	1 mm
Cell Pressure	-1 psig
Strip chart Recorder	
Type	Linear
Model	156
Range	1 Volt = 100 chartlines
Chart Speed	20 cm/hour

Table 3. Nominal Exposure Concentration

Group Number	Total Amount of Test Material Used (g)	Total Volume of Air (L)	Nominal Exposure Concentration (mg/L)
1	6.2	11840	0.5
2	19.7	15900	1.2

Table 4. Actual Exposure Concentration

Group Number	Sample Number	Exposure Concentration (mg/L)
1	1	0.5
	2	0.5
	3	0.5
	4	0.5
	5	0.5
	6	0.5
	7	0.5
	8	0.5
	9	0.5
	10	0.5
	11	0.5
	12	0.5
	13	0.5
	14	0.5
	15	0.5
	16	0.5
	17	0.5
	Mean	0.5
	S.D.	0.00

Group Number	Sample Number	Exposure Concentration (mg/L)
2	1	1.4
	2	1.3
	3	1.3
	4	1.3
	5	1.3
	6	1.3
	7	1.3
	8	1.3
	9	1.3
	10	1.3
	11	1.3
	12	1.3
	13	1.3
	14	1.3
	15	1.3
	16	1.3
	17	1.3
	Mean	1.3
	S.D.	0.02

S.D. = Standard Deviation

Table 5. Environment Measurements

Group Number	Temperature (°C) Mean	S.D.	Relative Humidity (%) Mean	S.D.	Air Flow Rate (L/min) Mean	S.D.	Oxygen Content (%)
1	24	0.0	2	0.0	40	0.0	20.8
2	23	0.0	6	0.4	50	0.0	21.0

S.D. - Standard Deviation

Table 6. Number of Animals Found Dead on Day of Study

Group	Study Day														
	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
2	0	0	2	1	0	0	1	0	0	1	1	2	1	1	NA

NA - Not applicable, all animals dead

Table 7. Body Weight Summary for Animals Found Dead on Study

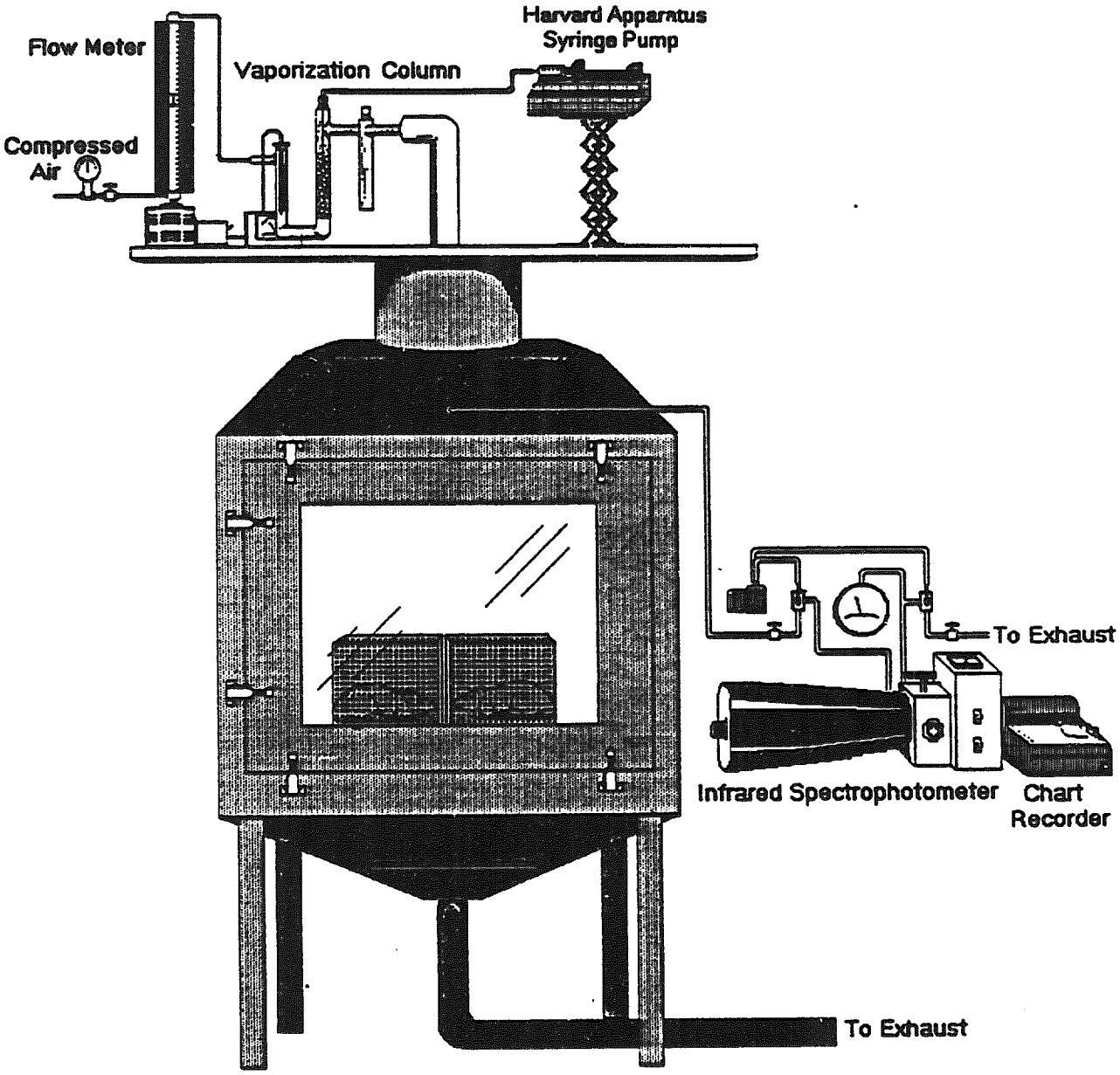
Group Number	Animal Number	Sex	Post-Exposure Day	Body Weight (g)
1	88219	F	13	82
2	88239	F	2	115
	88236	F	2	112
	88237	F	3	107
	88231	M	6	125
	88233	M	9	131
	88240	F	10	102
	88234	M	11	125
	88235	M	11	120
	88232	M	12	129
	88238	F	13	94

Table 8. Mean Group Body Weight (g) at Indicated Interval

Group Number	Sex	Pre-Exposure	Days Post-Exposure 7	14
1	M	204	178	192
	F	132	118	108
2	M	183	148	*
	F	132	117	*

*Animals found dead prior to measurement

Figure 1. Diagram of the Exposure and Analysis System



APPENDIX A
Test Material Information

Test Article Information

The test article was received from the Dow Corning Corporation on July 1, 1994. Presented below is the pertinent information on the test article.

Amount Received:	2 x 3 kg
Label Identification:	T2500
Lot No.:	140,273
Purity:	Not provided
Physico-Chemical Properties:	Pale yellow liquid
Stability:	Stable
Storage Conditions:	Room Temperature
IRDC Number:	11552

The Sponsor assumes responsibility for defining the identity, stability, strength, purity, and composition (or other characteristics) of the test article.

APPENDIX B
Individual Pharmacotoxic Signs

INDIVIDUAL PHARMACOTOXIC SIGNS
Immediately Post-Exposure

Males - Group number: 1		Day First Seen	Day Last Seen
88211	Decreased activity.	1	1
	Excessive lacrimation, Both eyes.	1	1
88212	Decreased activity.	1	1
	Excessive lacrimation, Both eyes.	1	1
88213	Decreased activity.	1	1
	Excessive lacrimation, Both eyes.	1	1
88214	Decreased activity.	1	1
	Excessive lacrimation, Both eyes.	1	1
88215	Normal/no visible abnormalities	1	1

INDIVIDUAL PHARMACOTOXIC SIGNS
Immediately Post-Exposure

Females - Group number: 1		Day First Seen	Day Last Seen
88216	Red/brown material around nose.	1	1
88217	Normal/no visible abnormalities	1	1
88218	Excessive lacrimation, Both eyes.	1	1
88219	Body surface stained, Nose.	1	1
	Excessive lacrimation, Both eyes.	1	1
88220	Decreased activity.	1	1
	Excessive lacrimation, Both eyes.	1	1

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INDIVIDUAL PHARMACOTOXIC SIGNS
Immediately Post-Exposure

Males - Group number: 2		Day First Seen	Day Last Seen
88231	Decreased activity.	1	1
	Red/brown material mouth.	1	1
88232	Decreased activity.	1	1
	Excessive lacrimation, Both eyes.	1	1
88233	Decreased activity.	1	1
	Excessive lacrimation, Both eyes.	1	1
88234	Decreased activity.	1	1
	Excessive lacrimation, Both eyes.	1	1
88235	Decreased activity.	1	1
	Red/brown material around nose.	1	1
	Excessive lacrimation, Both eyes.	1	1

INDIVIDUAL PHARMACOTOXIC SIGNS
Immediately Post-Exposure

Females - Group number: 2		Day First Seen	Day Last Seen
88236	Decreased activity.	1	1
	Excessive lacrimation, Both eyes.	1	1
88237	Decreased activity.	1	1
	Red/brown material mouth.	1	1
	Excessive lacrimation, Both eyes.	1	1
88238	Decreased activity.	1	1
	Red/brown material around nose.	1	1
88239	Decreased activity.	1	1
	Excessive lacrimation, Both eyes.	1	1
88240	Decreased activity.	1	1
	Red/brown material around nose.	1	1
	Red/brown material mouth.	1	1
	Excessive lacrimation, Both eyes.	1	1

INDIVIDUAL PHARMACOTOXIC SIGNS
(Study Days 2-15 Represent Post-Exposure Days 1-14)

Males - Group number: 1		Day First Seen	Day Last Seen	Days Sign Present
88211	Normal/no visible abnormalities	7	15	3
	Decreased activity,	2	14	11
	Gasping,	2	2	1
	Labored breathing,	3	5	3
	Slow Respiration,	3	4	2
	Red/brown material around nose,	2	4	3
88212	Normal/no visible abnormalities	7	8	2
	Decreased activity,	2	15	12
	Red/brown material around nose,	2	4	3
	Red/brown material mouth,	2	4	3
	Material around eye, Right eye,	11	15	5
88213	Normal/no visible abnormalities	7	15	9
	Decreased activity,	2	6	5
	Red/brown material around nose,	2	4	3
	Red/brown material mouth,	2	4	3
88214	Normal/no visible abnormalities	7	15	4
	Decreased activity,	2	13	10
	Wheezing,	3	3	1
	Red/brown material around nose,	2	4	3
	Red/brown material mouth,	2	4	3
88215	Normal/no visible abnormalities	8	9	2
	Decreased activity,	3	15	11
	Wheezing,	3	5	3
	Red/brown material around nose,	2	4	3
	Red/brown material mouth,	2	13	4

INDIVIDUAL PHARMACOTOXIC SIGNS
(Study Days 2-15 Represent Post-Exposure Days 1-14)

Females - Group number: 1		Day First Seen	Day Last Seen	Days Sign Present
88216	Normal/no visible abnormalities	7	8	2
	Decreased activity,	6	15	8
	Body surface stained, Anogenital region,	3	5	3
	Wheezing,	9	13	5
	Red/brown material around nose,	2	4	3
	Red/brown material mouth,	2	12	5
88217	Decreased activity,	2	15	12
	Body surface stained, Anogenital region,	3	15	10
	Red/brown material around nose,	2	4	3
	Red/brown material mouth,	2	4	3
88218	Normal/no visible abnormalities	7	11	5
	Decreased activity,	3	15	7
	Body surface stained, Anogenital region,	3	5	3
	Wheezing,	4	6	3
	Red/brown material around nose,	2	4	3
	Red/brown material mouth,	2	4	3
88219	Normal/no visible abnormalities	7	8	2
	Dead,	14	14	1
	Decreased activity,	2	13	10
	Body surface stained, Anogenital region,	3	5	3
	Body surface stained, Both forelimbs,	13	13	1
	Red/brown material around nose,	2	13	6
	Red/brown material mouth,	2	13	6
	Excessive lacrimation, Both eyes,	13	13	1
88220	Normal/no visible abnormalities	8	8	1
	Decreased activity,	2	15	13
	Body surface stained, Anogenital region,	3	4	2
	Wheezing,	3	3	1
	Red/brown material around nose,	2	4	3
	Red/brown material mouth,	2	15	7

INDIVIDUAL PHARMACOTOXIC SIGNS
(Study Days 2-15 Represent Post-Exposure Days 1-14)

Males - Group number: 2		Day First Seen	Day Last Seen	Days Sign Present
88231	Dead,	7	7	1
	Decreased activity,	2	6	5
	Body surface stained, Anogenital region,	2	6	5
	Body surface stained, Both forelimbs,	2	6	5
	Labored breathing,	6	6	1
	Wheezing,	4	5	2
	Red/brown material around nose,	2	6	5
	Red/brown material mouth,	2	6	5
	Corneal opacity, Both eyes,	6	6	1
88232	Dead,	13	13	1
	Decreased activity,	2	12	11
	Decreased defecation,	10	12	3
	Body surface stained, Anogenital region,	2	12	7
	Body surface stained, Both forelimbs,	9	12	4
	Body surface stained, Mouth,	11	12	2
	Gasping,	11	11	1
	Rapid Respiration,	6	6	1
	Slow Respiration,	10	12	3
	Wheezing,	2	5	2
	Red/brown material around nose,	2	12	7
	Red/brown material mouth,	2	10	4
	Excessive lacrimation, Both eyes,	2	12	2
	Eye discolored, Right eye,	3	4	2
88233	Dead,	10	10	1
	Decreased activity,	2	9	8
	Body surface stained, Anogenital region,	2	4	3
	Body surface stained, Both forelimbs,	2	9	5
	Body surface stained, Nose,	3	4	2
	Body surface stained, Right eye,	3	3	1
	Body surface stained, Right forelimb,	8	8	1
	Generalized swelling, Both forelimbs,	9	9	1
	Generalized swelling, Right forelimb,	8	8	1
	Rapid Respiration,	6	6	1
	Red/brown material around nose,	2	9	2
	Red/brown material mouth,	2	9	5
	Excessive lacrimation, Both eyes,	2	2	1
	Eye discolored, Right eye,	4	5	2

INDIVIDUAL PHARMACOTOXIC SIGNS
(Study Days 2-15 Represent Post-Exposure Days 1-14)

Males - Group number: 2 (Continued)		Day First Seen	Day Last Seen	Days Sign Present
88234	Dead,	12	12	1
	Decreased activity,	2	11	10
	Decreased defecation,	11	11	1
	No stool,	10	10	1
	Body surface stained, Anogenital region,	2	11	8
	Body surface stained, Both forelimbs,	2	11	6
	Body surface stained, Right forelimb,	9	9	1
	Gasping,	10	11	2
	Labored breathing,	4	4	1
	Rapid Respiration,	8	11	4
	Red/brown material around nose,	2	11	8
	Red/brown material mouth,	2	11	6
88235	Dead,	12	12	1
	Decreased activity,	2	11	10
	No stool,	10	11	2
	Body surface stained, Anogenital region,	2	11	10
	Body surface stained, Both forelimbs,	2	7	6
	Body surface stained, Distal tail,	5	11	7
	Body surface stained, Mouth,	11	11	1
	Gasping,	11	11	1
	Rapid Respiration,	6	9	4
	Slow Respiration,	10	10	1
	Wheezing,	2	5	4
	Penis extended,	10	11	2
	Red/brown material around nose,	2	11	10
	Red/brown material mouth,	2	10	6
	Corneal opacity, Right eye,	6	11	6
	Excessive lacrimation, Both eyes,	2	2	1
	Eye discolored, Right eye,	4	11	8

INDIVIDUAL PHARMACOTOXIC SIGNS
(Study Days 2-15 Represent Post-Exposure Days 1-14)

Females - Group number: 2		Day First Seen	Day Last Seen	Days Sign Present
88236	Dead,	3	3	1
	Decreased activity,	2	3	2
	Body surface stained, Anogenital region,	2	3	2
	Body surface stained, Both forelimbs,	2	3	2
	Body surface stained, Mouth,	3	3	1
	Cold to touch,	3	3	1
	Wheezing,	2	2	1
	Red/brown material around nose,	2	3	2
	Red/brown material mouth,	2	2	1
	Excessive lacrimation, Both eyes,	2	2	1
88237	Dead,	4	4	1
	Decreased activity,	2	3	2
	Body surface stained, Anogenital region,	2	3	2
	Body surface stained, Both forelimbs,	2	3	2
	Red/brown material around nose,	2	3	2
	Red/brown material mouth,	2	3	2
	Excessive lacrimation, Both eyes,	2	2	1
88238	Dead,	14	14	1
	Emaciated,	10	13	4
	Decreased activity,	2	13	12
	Decreased defecation,	12	13	2
	Body surface stained, Anogenital region,	2	13	6
	Body surface stained, Base of tail,	4	4	1
	Body surface stained, Both forelimbs,	2	5	4
	Body surface stained, Both hindlimbs,	4	5	2
	Cold to touch, Entire Body Surface,	13	13	1
	Gasping,	5	13	3
	Labored breathing,	6	8	3
	Wheezing,	10	11	2
	Red/brown material around nose,	2	5	4
	Red/brown material mouth,	6	12	7
	Eye closed, Both eyes,	13	13	1
88239	Dead,	3	3	1
	Decreased activity,	2	2	1
	Body surface stained, Anogenital region,	2	2	1
	Body surface stained, Both forelimbs,	2	2	1
	Gasping,	2	2	1
	Red/brown material around nose,	2	2	1
	Red/brown material mouth,	2	2	1
	Excessive lacrimation, Both eyes,	2	2	1

INDIVIDUAL PHARMACOTOXIC SIGNS
(Study Days 2-15 Represent Post-Exposure Days 1-14)

Females - Group number: 2 (continued)		Day First Seen	Day Last Seen	Days Sign Present
88240	Dead.	11	11	1
	Emaciated.	10	11	2
	Decreased activity.	2	11	10
	No stool.	10	11	2
	Body surface stained, Anogenital region.	2	11	10
	Body surface stained, Both forelimbs.	2	4	3
	Gasping.	10	11	2
	Rapid Respiration.	6	10	5
	Wheezing.	7	7	1
	Red/brown material around nose.	2	11	7
	Red/brown material mouth.	2	11	5
	Excessive lacrimation, Both eyes.	2	11	2
	Eye discolored, Right eye.	3	5	3

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APPENDIX C
Individual Body Weights

INDIVIDUAL BODY WEIGHTS (g)

Animal Number	Sex	Day of Study: Pre-Exposure	8	15
Group 1:				
88211	M	205	178	197
88212	M	201	177	189
88213	M	207	185	204
88214	M	206	179	193
88215	M	203	171	178
	(N)	5	5	5
	Means	204	178	192
	S.D.	3	5	10
88216	F	133	125	107
88217	F	134	123	120
88218	F	133	116	108
88219	F	130	112	*
88220	F	129	112	97
	(N)	5	5	4
	Means	132	118	108
	S.D.	2	6	10

S.D. = standard deviation
N = number of animals
* = Animal died prior to measurement

INDIVIDUAL BODY WEIGHTS (g)

Animal Number	Sex	Day of Study: Pre-Exposure	8
Group 2:			
88231	M	184	*
88232	M	183	155
88233	M	179	143
88234	M	187	147
88235	M	183	146
	(N)	5	4
	Means	183	148
	S.D.	3	5
88236	F	131	*
88237	F	130	*
88238	F	134	114
88239	F	135	*
88240	F	132	120
	(N)	5	2
	Means	132	117
	S.D.	2	4

S.D. = standard deviation
N = number of animals
* = Animal died prior to measurement
All animals found dead prior to day 14 measurement

APPENDIX D
Macroscopic Findings

GROUP, ANIMAL NUMBER	SEX	FATE[1]	TISSUE:	OBSERVATIONS:
Group 1				
88211	M	S	MACROSCOPIC:	
			All Other Tissues	- Within normal limits.
			Nasal Tissues	- Within normal limits.
88212	M	S	MACROSCOPIC:	
			All Other Tissues	- Within normal limits.
			Nasal Tissues	- Within normal limits.
88213	M	S	MACROSCOPIC:	
			All Other Tissues	- Within normal limits.
			Nasal Tissues	- Within normal limits.
88214	M	S	MACROSCOPIC:	
			Lung	- Discoloration, red, cardiac lobe, multifocal, mild.
			Nasal Tissues	- Within normal limits.
88215	M	S	MACROSCOPIC:	
			All Other Tissues	- Within normal limits.
			Nasal Tissues	- Within normal limits.

[1]FATE CODES: S=SCHEDULED SACRIFICE E=SACRIFICED IN EXTREMIS D=DIED ON STUDY

Individual Animal Data Record: Pathology
0 to Termination: RAT

GROUP, ANIMAL NUMBER	SEX	FATE[1]	TISSUE:	OBSERVATIONS:
Group 1				
88216	F	S	MACROSCOPIC:	
			Lung	- Discoloration, red, multiple lobes, multifocal, mild.
			Nasal Tissues	- Within normal limits.
88217	F	S	MACROSCOPIC:	
			All Other Tissues	- Within normal limits.
			Nasal Tissues	- Within normal limits.
88218	F	S	MACROSCOPIC:	
			Lung	- Discoloration, red, multiple lobes, multifocal, trace.
			Nasal Tissues	- Within normal limits.
88219	F	D	MACROSCOPIC:	
			Lung	- Discoloration, red, multiple lobes, diffuse, moderate.
			Nasal Tissues	- Within normal limits.
88220	F	S	MACROSCOPIC:	
			All Other Tissues	- Within normal limits.
			Nasal Tissues	- Within normal limits.

[1]FATE CODES: S=SCHEDULED SACRIFICE E=SACRIFICED IN EXTREMIS D=DIED ON STUDY

GROUP, ANIMAL NUMBER	SEX	FATE[1]	TISSUE:	OBSERVATIONS:
Group 2				
88231	M	D	MACROSCOPIC:	
			Eye	- Within normal limits.
				- Antemortem observation unconfirmed.
			Lung	- Discoloration, red, multiple lobes, diffuse, mild.
			Nasal Tissues	- Within normal limits.
88232	M	D	MACROSCOPIC:	
			Lung	- Discoloration, red, multiple lobes, multifocal, mild.
			Nasal Tissues	- Within normal limits.
88233	M	D	MACROSCOPIC:	
			Lung	- Discoloration, red, multiple lobes, multifocal, moderate.
			Nasal Tissues	- Within normal limits.
			Skin, Subcutis	- Within normal limits.
				- Antemortem observation unconfirmed.
88234	M	D	MACROSCOPIC:	
			Lung	- Discoloration, red, multiple lobes, multifocal, mild.
			Nasal Tissues	- Within normal limits.
88235	M	D	MACROSCOPIC:	
			Eye	- Discoloration, black, intraorbital, focal, right, mild; Corresponds to antemortem observation, discolored, black. The corneal opacity was not confirmed.
			Lung	- Discoloration, red, multiple lobes, multifocal, mild.
			Nasal Tissues	- Within normal limits.
			Penis	- Extended, no grade.
				- Corresponds to antemortem observation.
			Tail	- Discoloration, black, distal, focal, trace; Corresponds to antemortem observation, distal tail, black.
				- Absent, portion, distal, focal, trace; Corresponds to antemortem observation, distal tail, missing.

[1]FATE CODES: S=SCHEDULED SACRIFICE E=SACRIFICED IN EXTREMIS D=DIED ON STUDY

GROUP, ANIMAL NUMBER	SEX	FATE[1]	TISSUE:	OBSERVATIONS:
Group 2				
88236	F	D	MACROSCOPIC:	
			Lung	- Discoloration, red, multiple lobes, diffuse, severe.
			Nasal Tissues	- Within normal limits.
88237	F	D	MACROSCOPIC:	
			Lung	- Discoloration, red, multiple lobes, diffuse, severe.
			Nasal Tissues	- Within normal limits.
88238	F	D	MACROSCOPIC:	
			Animal/Whole Body	- Within normal limits.
				- Antemortem observation unconfirmed.
			Lung	- Discoloration, red, multiple lobes, focal, moderate.
			Nasal Tissues	- Within normal limits.
88239	F	D	MACROSCOPIC:	
			Lung	- Discoloration, red, multiple lobes, diffuse, severe.
			Nasal Tissues	- Within normal limits.
88240	F	D	MACROSCOPIC:	
			Animal/Whole Body	- Within normal limits.
				- Antemortem observation unconfirmed.
			Lung	- Discoloration, red, multiple lobes, multifocal, moderate.
			Nasal Tissues	- Within normal limits.

[1]FATE CODES: S=SCHEDULED SACRIFICE E=SACRIFICED IN EXTREMIS D=DIED ON STUDY

APPENDIX E

Protocol (without M.S.D.S.)

INTERNATIONAL RESEARCH AND DEVELOPMENT CORPORATION

PROTOCOL REVISION OR CLARIFICATION

Protocol Sheet No. 1 Study No. 416-098

TITLE: ACUTE INHALATION TOXICITY EVALUATION ON TRIETHOXYSILANE IN RATS

ITEM	JUSTIFICATION
1.	Study initiation.
2.	Study scheduled complete.
3.	Rationale for use of animals.
4.	Body weight adjustment for Fischer Rats.

ITEM	PROTOCOL REVISION OR CLARIFICATION
1.	Conduct study in accordance with the attached protocol.
2.	Page 2, Section VIII. Proposed Date of First Exposure: July 13, 1994 Proposed Date of Terminal Necropsy (First Group): July 27, 1994 Proposed Date of Report (Audited Draft): To be scheduled (8 weeks after study termination or last necropsy)
3.	Page 4, Section X.M. The current state of scientific knowledge does not provide acceptable alternatives, in vitro or otherwise, to the use of live animals to accomplish the purpose of this study.

Study Director Roger J. Hilaski, M.A.

Roger Hilaski 6/20/94

Signature Date

IR90-49-5

0044

INTERNATIONAL RESEARCH AND DEVELOPMENT CORPORATION

PROTOCOL REVISION OR CLARIFICATION

Protocol Sheet No. 1 Study No. 416-098

TITLE: ACUTE INHALATION TOXICITY EVALUATION ON TRIETHOXYSILANE IN RATS

ITEM	PROTOCOL REVISION OR CLARIFICATION (continued)
4.	Page 3, Section X.D.E. Age at the start of the study will be approximately 8 weeks with body weight appropriate for this strain and age.

Study Director Roger J. Hilaski, M.A.

Roger Hilaski 6/20/94

Signature Date

I. STUDY TITLE

Acute Inhalation Toxicity Evaluation on Triethoxysilane in Rats

II. PURPOSE OF THE STUDY

The purpose of this study is to evaluate the acute toxicity of an experimental compound when administered via the inhalation route according to the Guidelines of the Organization for Economic Cooperation and Development (Acute Inhalation Toxicity, No. 403) issued May 12, 1981 and the Environmental Protection Agency: Toxic Substances Control Act Test Guidelines, Part 798 - Health Effects Testing Guidelines, subpart B., Section 798.1150, September 1985.

III. STUDY NUMBER

416-098

IV. TESTING FACILITY

International Research and Development Corporation
Mattawan, Michigan 49071

V. SPONSOR

Dow Corning Corporation
2200 West Salzburg Road
Auburn, MI 48611

VI. SPONSOR'S REPRESENTATIVE

Waheed Siddiqui, Ph.D.
Tel: 517-496-4884

VII. IRDC PERSONNEL RESPONSIBILITIES

Study Director:	Roger J. Hilaski, M.S. Staff Toxicologist, Inhalation Toxicology
Alternate Study Director:	Charles E. Ulrich, B.S. Director, Inhalation Toxicology
Director of Research:	C. Spencer Streett, V.M.D.., A.C.V.P. Diplomate
Associate Director of Research:	James L. Schardein, M.S., A.T.S.
Director, Corporate Regulatory Affairs:	William M. Harrison, B.S.
Director, Quality Assurance:	Margery J. Wirth, B.S.
Director, Planning and Scheduling:	Robert E. Drafta, B.A.
Director, Analytical Toxicology:	Joseph H. Thorstensen, Ph.D.
Director, Clinical Laboratory Medicine:	Larry H. Hulsebos, D.V.M., A.C.L.A.M. Diplomate

VII. IRDC PERSONNEL RESPONSIBILITIES (continued)

Director, Pathology Division:	Johnnie J. Eighmy, D.V.M., M.S., A.C.V.P. Diplomate
Director, Pathology Services:	Karen S. Regan, D.V.M., A.C.V.P. Diplomate
Technical Reports Coordinator:	Alice J. West, B.S.
Biostatistician:	Rebecca L. Miller, M.S.

VIII. SCHEDULE

Proposed Date of First Exposure:

Proposed Date(s) of Terminal Necropsy:

Proposed Date of Report (Audited Draft):

The study initiation date is defined as the date on which the Study Director signs and dates Protocol Sheet No. 1. The study completion date is defined as the date on which the Study Director signs and dates the Final Report.

IX. TEST MATERIAL DATA

A. Identification: Triethoxysilane

B. IRDC Number:

C. Lot Number:

D. Batch Number:

E. Physico-Chemical Properties: Colorless to yellow liquid

F. Purity: Available from Sponsor

G. Shelf Life:

H. Storage Conditions: See attached MSDS

I. Safety Precautions: See attached MSDS

J. Stability: Stable

K. Source: The experimental compound will be provided by the Sponsor.

L. Amount Required: At least five (5) kilograms of five (5) liters will be required for solids or liquids, respectively.

IX. TEST MATERIAL DATA (continued)

M. Test Article Return: Any remaining unused test article will be returned to the Sponsor at study completion to the following address:

Waheed Siddiqui, Ph.D.
Dow Corning Corporation
Health & Environmental Sciences
2200 W. Salzburg Road
Auburn, MI 48611

If no address is provided, the test article will be returned to the address indicated in Section V (The Study Director will be notified prior to each shipment).

X. TEST ANIMALS

A. Species: Rat

B. Strain: Fisher Rats
CDF® (F-344)/CrlBR

C. Source: Charles River Laboratories
9801 Shaver Road
Portage, Michigan 49081

D. Age at Start of Study: Approximately six (6) weeks

E. Body Weight: Individual animal body weight for each will be within the ranges indicated below. All individual animals of a particular sex within a given group will be within ± 20% of the mean weight for that sex and all group means for a particular sex will be within ± 20%.

Males: 200 - 300 grams
Females: 150 - 225 grams

F. Method of Identification: Individual numbered metal ear tag.

G. Number on Study: Between ten (10) and one hundred (100)

H. Housing: Individually caged during both the pre-exposure and the post-exposure observation periods. Colony room temperature and humidity will be between eighteen (18) and twenty-six (26) degrees centigrade and forty (40) to seventy (70) percent relative humidity. The photo period will be controlled for 12 hours light and 12 hours dark.

I. Quarantine: At least seven (7) days

J. Reason for Selection: The rat is a universally used model for evaluating acute toxicity.

X. TEST ANIMALS (continued)

K. Justification for Number on Study: This study was designed to use the fewest number of animals possible, consistent with the objective of the study, the scientific needs of the Sponsor, contemporary scientific standards and in consideration of applicable regulatory requirements.

L. Randomization: The rats used for this study will be selected from a colony maintained for acute work. The animals will appear healthy and free of any signs of disease prior to selection for this study. When two (2) or more groups are to be exposed on the same day, the animals will be randomized into the various groups utilizing simple randomization (Standard Randomization Procedure C).

When only one (1) group is to be exposed on a given day, formal randomization will not be required. Each animal will be given a permanent animal number and an ear tag with that number will be placed on the animal.

XI. DIET AND DRINKING WATER

A. Basal Laboratory Diet Data

1. Basal Diet: Certified Pelleted Rodent Chow® #5002, Purina Mills, Inc., ad libitum except during actual exposures.

2. Identification: Each lot utilized will be identified and recorded.

3. Contaminant Levels: Neither the Sponsor nor the Study Director is aware of any potential contaminants likely to be present in the certified diet which would interfere with the results of this study. Therefore, no analyses other than those routinely performed by the feed supplier will be conducted.

B. Drinking Water

Tap water will be supplied ad libitum except during actual exposures.

The drinking water used for test animals will be monitored for specified contaminants at periodic intervals according to IRDC Standard Operating Procedures. Neither the Sponsor nor the Study Director is aware of any potential contaminants likely to be present in the drinking water which would interfere with the results of this study. Therefore, no analyses other than those mentioned in this protocol will be conducted.

XII. STUDY DURATION

The time required to conduct this study will vary from approximately two (2) weeks, when only Phase I is required, up to approximately six (6) weeks when Phase II is also required.

XIII. METHOD OF ADMINISTRATION OF THE TEST MATERIAL

Since inhalation is considered a potential route for human exposure, the compound will be administered via the inhalation route utilizing whole body exposure methods.

XIV. EXPERIMENTAL DESIGN

This study will be divided into two (2) phases. During Phase I a single group of five (5) male and five (5) female rats will be exposed for four (4) hours to an actual concentration slightly greater than 0.5 mg/L (750 ppm). If no animals die during a fourteen (14) day observation period (sexes combined), then the study will be terminated and reported, and Phase II will not be required. However, if any animals die, the Sponsor will be contacted and the need for additional exposure levels will be determined. When additional exposure levels are required to better define the acute toxicity of the test material, Phase II will be conducted.

If a solvent is required to generate the material, then a solvent control group will be added to the design.

A. Exposure Methods

Exposures will be conducted in fifty-four (54) liter all glass or one-hundred-sixty (160) liter stainless steel and glass exposure chambers. The 4-hour exposure will be measured from the end of the t_{99} equilibration time. The chambers will be operated under dynamic conditions where the chamber ventilation air is supplied by either the HVAC system which is separate from the general laboratory systems or by in-house compressed air. Chamber temperature and humidity will be monitored continuously and will be within twenty (20) to twenty-four (24) degrees centigrade and thirty (30) to seventy (70) percent RH if possible, considering the requisite exposure conditions. Chamber ventilation rate will be at least twelve (12) air changes per hour and will be monitored continuously. Chamber airflow rate, temperature and relative humidity will be recorded at least four (4) times during each exposure. The oxygen content will be maintained at nineteen (19) percent or greater, and will be measured once during each exposure (if possible, considering potential interaction between the O_2 sensor and the test material). All animals will be caged individually during the exposure.

XIV. EXPERIMENTAL DESIGN (continued)

B. Exposure Atmosphere Generation Methods

For liquids, exposures will be to a liquid droplet aerosol of the compound unless a vapor exposure is specifically requested.

Details of generation system methodologies cannot be defined until development work with the test material is completed. Therefore, this will be recorded in the Study Notes after preliminary methods evaluations are conducted.

C. Method for Determination of Exposure Concentrations

Actual and nominal chamber concentrations will be determined for all exposures. For materials with a significant vapor pressure and for all vapor exposures, a specific analytical evaluation will be required. The analytical method will be supplied by the sponsor. Additional costs will be incurred for these analytical determinations. All results will be evaluated in terms of the actual measured concentrations. At least four (4) determinations will be made during each exposure.

D. Methods for Determination of Aerosol Particle Size

Particle size determinations will be conducted once (1X) during each exposure utilizing an Andersen Cascade Impactor. Aerosol size will be expressed in terms of the mass median aerodynamic diameter (MMAD) and the geometric standard deviation (GSD).

E. Observations for Pharmacotoxic Signs

Since all animals cannot be adequately observed during exposures to high aerosol concentrations, observations for pharmacotoxic signs will be conducted on all animals immediately on removal from the exposure system. During the fourteen (14) day post-exposure observation period, the animals will be observed twice (2X) daily, once (1X) for mortality and once (1X) daily for pharmacotoxic signs.

F. Body Weights

Body weights will be recorded just prior to exposure and on days seven (7) and fourteen (14) post-exposure. Animals will also be weighed when found dead. When an extended post-exposure observation period is required, body weights will continue to be recorded at weekly intervals.

XIV. EXPERIMENTAL DESIGN (continued)

G. Necropsy

All animals which die during the exposure, during the observation period or are euthanized at the termination of the study, will undergo a complete necropsy. Euthanasia will be by intraperitoneal sodium pentobarbital and exsanguination via the abdominal aorta. The trachea will be exposed and clamped such that the lungs can be removed and examined in an inflated state. All major organ systems in the thoracic and abdominal cavities will be observed for gross abnormalities and then the carcass will be discarded. No tissues will be preserved.

XV. STATISTICAL ANALYSIS

When appropriate, the concentration mortality data may be statistically analyzed for the LC_{50} and its confidence limits by one of the following methods:

A simplified method of evaluation dose-effect experiments
J. T. Litchfield, Jr. and F. Wilcoxon
J. Pharmacol. and Expt. Therp.
Vol. 96, 1949

The determination of the dosage-mortality curve from small numbers
Bliss
Quart. J. Pharm. Pharmacol.
Vol. 11, 1938

XVI. REPORT

The report will contain a detailed description of the experimental design and methods. Individual and mean body weight data along with standard deviations on surviving animals will be provided. Narrative or tabular style data on pharmacotoxic signs and macroscopic abnormalities observed at necropsy will be provided. Exposure concentrations will be reported as a mean and standard deviation, or other appropriate summarization method, while particle size data will be reported as log size-probability plot, typical for the exposure conducted. Two (2) copies of the report will be provided.

XVII. PERSONNEL HEALTH AND SAFETY

Safety precautions appropriate for materials of unknown toxicity potential will be employed in the handling of the test compound unless indicated otherwise in Section IX.

XVIII. DATA RETENTION

All raw data, documentation, records, protocols, test article reserve sample(s), and final reports generated as a result of this study will be retained at IRDC and will be made available for inspection upon

XVIII. DATA RETENTION

request by authorized personnel of the Sponsor for a period of 5 years following the completion of the study (final report issue date). Study specimens, if collected for this study, will be retained by IRDC for a minimum period of 1 year, to a maximum of 2 years, following the completion of the study (final report issue date).

Study specimens include wet tissues, blocks and microscopic slides. Specimens may be returned to the Sponsor or retained at IRDC. Retention of materials after the times stated above will be subject to future contractual agreements between the Sponsor and IRDC.

The charges for storage of study specimens for this study do not include any costs for handling and shipping at final disposition.

All unused test article, except the retention sample, will be returned to the Sponsor after completion of the study.

XIX. QUALITY ASSURANCE

This study will be subjected to randomly selected Quality Assurance inspection in accordance with IRDC Standard Operating Procedures, and the final report will be reviewed by the IRDC Quality Assurance Department. Study Quality Assurance inspection records will be made available to the Sponsor during Sponsor visits to IRDC.

XX. GOOD LABORATORY PRACTICES

The study will be conducted in accordance with the OECD Principles of Good Laboratory Practice (adopted May 12, 1981) and the EPA-TSCA Good Laboratory Practice Standards.

XXI. STATEMENT OF COMPLIANCE

The final report will include a statement signed by the Study Director addressing whether the Final Report accurately reflects the raw data obtained during the performance of the study and whether there were significant deviations from the Good Laboratory Practice Regulations which affected the quality or integrity of the study. If deviations are encountered that will affect the quality or integrity of the study, each deviation will be described in detail.

XXII. ALTERATION OF DESIGN

Alterations of this protocol may be made as the study progresses. No changes will be made without the specific request or consent of the Sponsor. In the event that the Sponsor authorizes a protocol change verbally, such change will be honored by IRDC. However, it then becomes the responsibility of the Sponsor to follow such verbal change with a written verification. Changes or clarifications to this protocol will be documented in the study records and signed by the Study Director.

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XXIII. DECLARATION OF INTENT

This study should be listed on the IRDC Quality Assurance Master Schedule for:

A. U.S. Environmental Protection Agency

FIFRA _____

TSCA X

B. Organization for Economic Cooperation and Development OECD X

C. U.S. Food and Drug Administration FDA _____

D. None of the above _____

XXIV. STATEMENT OF ANIMAL CARE AND USE COMPLIANCE

IRDC is committed to being in compliance with all applicable regulations governing the care and use of laboratory animals. In order to ensure compliance, this protocol will be reviewed by the Institutional Animal Care and Use Committee (IACUC) before the study starts.

Approved by Sponsor

DOW CORNING CORPORATION

By: W Siddiqui
Waheed Siddiqui Ph.D.

Title: Associate Toxicology Scientist

Date: 2/16/94

Prepared by

INTERNATIONAL RESEARCH AND DEVELOPMENT CORPORATION

By: Roger Hilaski
Roger J. Hilaski, M.A.

Title: Staff Toxicologist, General Toxicology

Date: 2-14-94

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INTERNATIONAL RESEARCH AND DEVELOPMENT CORPORATION

PROTOCOL REVISION OR CLARIFICATION

Protocol Sheet No. 2 Study No. 416-098

TITLE: ACUTE INHALATION TOXICITY EVALUATION ON TRIETHOXYSILANE IN RATS

ITEM	JUSTIFICATION
1.	Test Material Data addition.

ITEM	PROTOCOL REVISION OR CLARIFICATION
1.	Page 2, Section IX. B. IRDC Number: 11552 C. Lot Number: 140, 273 D. Batch Number: not applicable F. Purity: not available from Sponsor G. Shelf Life: Through the end of the study N. Sponsor assumes responsibility for appropriately defining the identity, strength, purity composition (or other characteristics), and stability of the test article.

APPROVED BY:

S Hiddlyn 7/25/94

Sponsor's Representative Date

Study Director Roger J. Hilaski, M.A.

Roger Hilaski 7/11/94

Signature Date

IR90-49-5

0055

INTERNATIONAL RESEARCH AND DEVELOPMENT CORPORATION

PROTOCOL REVISION OR CLARIFICATION

Protocol Sheet No. 3 Study No. 416-098

TITLE: ACUTE INHALATION TOXICITY EVALUATION ON TRIETHOXYSILANE IN RATS

This amendment is to become effective as of July 21, 1994

ITEM	JUSTIFICATION
1.	Clarification of Test animal age.
2.	Determination of Exposure Concentration.

ITEM	PROTOCOL REVISION OR CLARIFICATION
1.	Age at the start of the study will be approximately 9 weeks with body weight appropriate for this strain and age.
2.	Actual exposure concentrations will be determined by Infrared (IR) Spectroscopy. The exposure concentration will be continuously monitored.

APPROVED BY:

S Hiddlyn 8/3/94

Sponsor's Representative Date

Study Director Roger J. Hilaski, M.A.

Roger Hilaski 7/22/94

Signature Date

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INTERNATIONAL RESEARCH AND DEVELOPMENT CORPORATION

PROTOCOL REVISION OR CLARIFICATION

Protocol Sheet No. 4 Study No. 416-098

TITLE: ACUTE INHALATION TOXICITY EVALUATION ON TRIETHOXYSILANE IN RATS

PROTOCOL DEVIATIONS

1. The animals were ordered specifically for this study from: Charles River Kingston
RTE 209
Stone Ridge NY 12484

The protocol state the source as a stock colony purchased from: Charles River Laboratories
Portage, MI

2. Group 1 animals were acclimated for 16 days prior to exposure. The protocol stated at least 7 days acclimation.

3. The females averaged 132 gms at the study start. The protocol stated 150 - 225 gms, protocol amendments stated animals of 8 and 9 weeks of age with appropriate body weight. The animals were 57 and 66 days old at the study start.

4. Relative humidity in the chamber during the exposures was 2% and 6% for Groups 1 and 2, respectively. The protocol stated 30% - 70% relative humidity during exposure.

In the opinion of the Study Director, the above minor protocol deviations did not affect the quality or integrity of the study.

APPROVED BY:

[signature] 11/3/94
Sponsor's Representative Date

Study Director Roger J. Hilaski, M.A.

Roger Hilaski 10/24/94
Signature Date

APPENDIX F
Comments on Study Data

Comments on Study Data

This study was conducted in conformance with the protocol, IRDC Standard Operating Procedures and in compliance with the EPA TSCA Good Laboratory Practice Standards 40 CFR Part 792 effective September 18, 1989 and the OECD Principles of Good Laboratory Practice adopted May 12, 1981.

Animals were received from Charles River Kingston, not Charles River Portage as stated in the protocol. The animals used were specifically ordered for the study.

Day 1 post exposure temperature and humidity were not recorded on 7/22/94.

Group 2 animals were approximately 8 weeks of age at start of dosing.

No record of animal services activities were available for 8/10/94 and 8/11/94.

The purity of the test article was not available.

Only one person signed for the transcription of the antemortem information to the pathology record sheets for three animals.

In the opinion of the Study Director, these minor deviations did not affect the quality or integrity of the study.

GLOSSARY

Actual concentration - An independent measure of the amount of test article (per sample volume, e.g., mg/L) present in the exposure chamber. It is based upon analytical determination (usually gravimetric or instrumental) of the test article.

Concentration - Amount of a given material in a given volume of air (or gas); e.g., mg/L, mg/m^3 or ppm.

Desired concentration - The target exposure level of test article (per volume unit, e.g., mg/L) selected for each exposure group.

Exposure atmosphere types -

Vapors: The gas form of any substance which is usually a liquid or solid at room temperature.

Gases: A substance which is neither liquid nor solid at room temperature, has a very low density and viscosity, relatively great expansion and contraction with changes in pressure and temperature, diffuses readily and spontaneously distributes uniformly throughout any container.

Aerosols: Solid or liquid particles dispersed or suspended in air or a gas, e.g., mist, spray, fog, smoke, etc.

Exposure day - Defined as the day or days when an exposure was conducted for a study.

Exposure duration - The time interval during which the animals were exposed to the test article, e.g., 1 hour, 4 hours, etc.

Geometric standard deviation (GSD) - A number defining the dispersion of the aerosol size distribution.

Inhalable particles - Those materials that are deposited anywhere in the respiratory tract.

Mass median aerodynamic diameter (MMAD) - A measurement of aerosol size based on the inertial/aerodynamic properties of the particles. The measurements are usually made with a cascade impactor.

Nominal concentration - A gross estimate of exposure concentration based upon test article usage. The total amount of test article used during a given exposure day divided by the total volume of air passed through the chamber during the exposure.

Respirable particles - Those materials that are deposited in the gas-exchange region of the lung.

Respiratory tract - Composed of the conducting airway including the nose, mouth, pharynx, trachea, bronchi, bronchioles and alveoli.

Saturated vapor concentration - The concentration (usually in ppm) of a vapor in equilibrium with its liquid at a given temperature.

psig - Pounds per square inch, gauge

psia - Pounds per square inch, absolute

T_{99} - The time required for an exposure system to change from an equilibrated state to attain 99% of a new concentration level. This time interval is referred to as "chamber equilibrium time", is usually expressed in minutes and is calculated as follows:

$$T_{99} = 4.60 \times \frac{\text{Chamber volume}}{\text{Chamber flow rate}}$$